

REMARKS

Claims 55-77 remain in this application.

1. Submitted herewith is a Supplemental IDS that addresses the objections raised by the Examiner.

2. An amended Abstract is submitted herewith.

4.(h) Claim 58 has been amended to change "compounds" to compound.

5. With regard to 35 USC §112 anticipation rejection labeled paragraph 6 of the last office action, the Examiner is incorrect. It is true that the proviso at the end of claim 55 does not exclude the species if R¹ is H; R² is H; R³ is H; A is -CH=CH-; D is -(CH₂)₅-N(CH₂CH₃)-; and G is -CH₂-Ph. However, there does not exist the need to exclude such a species because according to the definition on page 4, line 6 from below to page 5, line 2, D includes C₃-C₁₂ alkylene (i.e., for example a C₆-alkylene) wherein one methylene unit is isosterically replaced by NR⁷ wherein R⁷ may be ethyl, however, with the exception of the (G)-terminal methylene group. Therefore -(CH₂)₅-N(CH₂CH₃)- is not included in the definition of D. However, the proviso at the end of claim 55 has been amended as follows: wherein if R¹, R² and R³ are hydrogen, R is not -CH=CH-, D is not -(CH₂)₅-N(CH₂CH₃)-CH₂- and G is not phenyl. This proviso excludes the species disclosed in Ishihara et., Chem. Pharm. Bul.

7.(c) Claim 72 has been amended to indicate that "R⁷ has the same meaning as R⁶".

e) Claim 73 has been amended to show the point of attachment of G4 by adding a bond before NR¹¹.

f) Claims 56, 57, 60, 70, 71, 72, 73, 75, 76 and 77 have been amended to change " R^{11} " and the group $-NR^8R^9$ " to "and R^{11} ".

av) Claim 69 has been amended to make it dependent on claim 66 and not on 68.

ax) Claim 73 has been amended to include "m is 0 or 1", before the paragraph starting with " R^8 is selected from".

az) Claim 73 has been amended to change " $=CR^9R^{10}$ " to " $=CR^8R^9$ ".

ba) Claim 74 has been amended to change "N" to n.

be) Claim 75 has been amended include "m is 0 or 1" before the paragraph starting with " R^8 is selected from".

bf) Claim 75 has been amended to include " R^{11} has the same meaning as R^4 , but is selected independently thereof;" before the paragraph beginning with "G is selected from the group".

bh) Claim 75 has been amended to delete "and in ring system $=CR^9R^{10}$ ". Further Claim 76 has been amended to delete "and $=CR^8R^9$ ".

bi) Claim 77 has been amended to add a bond before NR^{11} in the formula for G.

8. Claim 70 has been amended to delete "and combinations thereof".

9. Claim 73 has been amended to change "sulfonic acid esters, and mixtures thereof," to "and sulfonic acid esters".

10.a) Claim 55 has been amended to change "CH-CH-" to "-CH=CH-" and replace "R₁, R₂ and R₃" "by R¹, R² and R³".

b) Claim 56 has been amended to change "consiting" to "consisting".

c) Claim 57 has been amended to change "consiting" to "consisting" in the definition of R⁸.

d) Claim 57 has been amended to delete "R³" in the last paragraph and change "substituted" to "substituents".

e) Claim 58 has been amended to change "naphthylmethyaminocarbonylamino" to "naphthylmethylaminocarbonylamino" and "biphenylylamino" to "biphenylaminocarbonylamino".

f) Claim 60 has been amended to replace "-CH=CH-" for "CH=CH-" in the definition of A of the proviso and to include bonds before and after "(CH₂)₅" in the definition of D thereby changing it to "-(CH₂)₅-". Further "R₁, R₂ and R₃" have been replaced by "R¹, R² and R³".

g) Claim 70 has been amended to replace "-CH=CH-" for "CH=CH-" in the definition of A of the proviso and to include bonds before and after "(CH₂)₅" in the definition of D thereby changing it to "-(CH₂)₅-". Further "R₁, R₂ and R₃" have been replaced by "R¹, R² and R³".

h) Claim 73 has been amended to delete "hologenated" in the definition of L.

i)+j) Claim 73 has been amended by deleting materials starting from "G² is =CR⁸R⁹" to "n is 0, 1 or 2".

k) Claim 73 has been amended to replace "X¹-(CH₂)_n-(CR⁹R¹⁰)_m-R⁸" by "-X-(CH₂)_m-(CR⁹R¹⁰)_m-R⁸", to change "X¹" to "X", to delete "O or S" as examples for X¹, and to replace "X¹" by "X".

l) Claim 74 has been amended to indicate that "R¹¹" has the same meaning as R⁴, but it selected independently thereof;"

m) Claim 74 has been amended to change "N" into "n".

n) Claim 75 has been amended to change "consiting" to "consisting" in the definition of R⁸.

o) Claim 76 has been amended as follows:

- i) "are reacted" has been deleted;
- ii) the following has been added, "which intermediate is then reacted with a compound of formula (VII), H-NR⁸R⁹ (VII);"
- iii) the following has been added before the definition of G: "X is NR¹¹";

p) Claim 76 has been amended to change "consiting" to "consisting" in the definition of R⁸.

q) Claim 76 has been amended to delete material and both occurrences of "R¹⁰".

r) Claim 76 has been amended to include a bond in the definition of G before "NR¹¹".

s) Claim 76 has been amended to include the following before the paragraph concerning the definition of G, "R¹¹ has the same meaning as R⁴, but is selected independently thereof;"

t) Claim 76 has been amended to delete "m and the substituents".

u) Claim 77 has been amended to change "consiting" to "consisting" concerning the defining of R⁸.

v) Claim 77 has been amended to delete "R¹⁰" and its definition.

w) Claim 77 has been amended to include the following paragraph, "R¹¹ has the same meaning as R⁴, but is selected independently thereof:".

x) Claim 77 has been amended to delete "m and the substituents" and include "X is NR¹¹ before the definition of G.

The Examiner has rejected claim 55, 60 and the claims dependent thereon under 35 USC §102 (b) and (e). The Examiner however is incorrect that the objected claims were anticipated by the newly cited documents as will be outlined as follows:

11. The compounds and compositions disclosed in Nadzan et al, U.S. Patent No. 4,971,978, do not anticipate the rejected claims because D in the present application cannot be -CH(C(O)-N(C₅H₁₁)₂)-CH₂-CH₂-C(O)- as C₃-C₁₂-alkylene in the definition of D may not be substituted by (C(O)-N(C₅H₁₁)₂).

12. The compounds disclosed in Spatz et al., U.S. Patent No. 4,892,952 do not anticipate the compounds and compositions of the present invention because D cannot be -CH₂-CH₂-O-, as the isoteric replacement of the C₃-C₁₂-alkylene may not occur in the (G)-terminal methylene group.

13. Goto et al., JP Patent No. 02-212459 does not anticipate the compounds and compositions of the present invention because D cannot be $-(CH_2)_5-N(CH_2CH_3)-$ as the isosteric replacement of C_3-C_{12} -alkylene may not occur in the (G)-terminal methylene group.

14. The teaching by Saito et al., J. Enzyme Inhib., cannot anticipate the compounds and compositions of the present invention because D cannot represent $-CH(CO_2H)-CH_2-CH_2-$ as carboxylic acid does not represent a substituent of the C_3-C_{12} -alkylene group.

15. Koenig et al, EP 477 499, cannot anticipate the compounds and compositions of the present invention because D cannot be $-CH(CH_2OBU-t)-C(O)-NH-CH(CO_2BU-t)-$ as C_3-C_{12} -alkylene in the definition of D may not be substituted neither by t-butoxymethyl nor by t-butoxycarbonyl.

16. Hashimoto et al., Pharm Res., does not anticipate the compounds and compositions of the present invention because D cannot be $-CH(CO_2H)-(CH_2)-$, as D does not comprise C_2 -alkylene and also may not be substituted by a carboxylic acid group.

17. Kukkola et al., Bioorg, Med. Chem. Lett, does not anticipate the compounds and compositions of the present invention because D cannot be $-CH_2(CH_2-SH)-CH_2-$, as D does not comprise CH_2 C_2 -alkylene, nor may it be substituted by thiomethyl.

18. Itoh et al., WO 96/16981, does not anticipate the compounds and compositions of the present invention because D cannot be $-CH(CH_2-Ph)-C(O)-N(CH_3)-$, as (i) C_3-C_{12} -alkylene may not be substituted by benzyl and (ii) and isosteric

replacement may not occur for the (G)-terminal methylene group.

19. Adams et al, WO 96/22966 does not anticipate the compounds, compositions and method of use of the compounds of the present invention because D cannot be $-\text{CH}(\text{i-Bu})-\text{CO}-\text{NH}-\text{CH}(\text{CH}_2-\text{CO}_2\text{H})-$, as D for the definition of C_3-C_{12} alkylene may neither be substituted by (i) isobutyl nor by (ii) $\text{CH}_2-\text{CO}_2\text{H}$.

20. Myers et al., J. Am. Chem. Soc. Does not anticipate the compounds of the present invention because D cannot represent $-\text{CH}(\text{CH}_3)-\text{CH}(\text{OH})-$ as the definition for D does not allow C_2 -alkylene (which may be substituted).

21. Fujisawa et al., WO 97/41104, cannot anticipate the compounds and compositions of the present invention because D may not be $-\text{CH}_2-\text{C}(\text{O})-\text{N}(\text{CH}_3)-$, as the isoteric replacement of a methylene unit might not occur for the (G)-terminal methylene group.

22. Audia et al., WO 98/22494, cannot anticipate the compounds and compositions of the present invention because D cannot be $-\text{CH}(\text{CH}_3)-\text{C}(\text{O})-\text{NH}-\text{CH}(\text{CO}-\text{O}-\text{CH}_3)-$ as the definition of D does not allow a substitution by methoxycarbonyl.

23. Santangelo et al. U.S. Patent No. 5,760,241, cannot anticipate the compounds and compositions of the present invention because D may not be $-\text{CH}(\text{CO}_2\text{H})-\text{CH}_2-$ as the definition for D does not allow C_2 alkylene nor does it allow the substitution by a carboxylic acid group.

24. Hayes et al., WO 98/34111, cannot anticipate the compounds and compositions of the present invention because D

cannot represent $-\text{CH}(\text{CONH}_2)-\text{CH}_2-$ as D may not be C_2 -alkylene, nor may it be substituted by aminocarbonyl.

25. Palmer et al., U.S. Patent No. 5,977,302, cannot anticipate the compounds of the present invention because D may not be $-\text{CH}(\text{CH}_2\text{OH})-\text{CO}-$, as D cannot be substituted by hydroxymethyl.

26. Sham et al. WO 97/21685, cannot anticipate the compounds compositions and method of use of the compounds of the present invention because D can neither be $-\text{CH}(\text{CH}_2\text{-Ph})-\text{CH}(\text{OH})-\text{CH}_2-\text{CH}(\text{NH}-\text{CO}-\text{OBu-t})-$ nor $-\text{CH}(\text{CH}_2\text{Ph})-\text{CH}(\text{OH})-\text{CH}_2-\text{CH}(\text{NH}_2)-$. The definition for D does not allow the substitution with any of the following residues: benzyl, t-butoxycarbonylamino or amino.

27. Abelman et al., WO 96/19493, cannot anticipate the compounds and compositions of the present invention because A not be $-\text{CH}_2-\text{CH}(\text{NH}_2)-$ because the definition of A does not allow an isosteric substitution adjacent to the amide group.

28. Hu et al., U.S. Patent No. 6,166,052, cannot anticipate the compounds and compositions of the present invention because A cannot be

$-\text{CH}_2-\text{CH}(\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}(\text{CH}_3)_2)-$,
 $-\text{CH}_2-\text{CH}(\text{N}(\text{Me})-(\text{CH}_2-\text{CH}_2-\text{CH}(\text{CH}_3)_2))-$,
 $-\text{CH}_2-\text{CH}(\text{N}(\text{Me})(i\text{-Bu}))-$,
 $-\text{CH}_2-\text{CH}(\text{N}(\text{Me})\text{CH}_2-\text{CH}_2-\text{CH}(\text{CH}_3)_2)-$, and
 $-\text{CH}_2-\text{CH}(\text{NH}_2)-$

The following substituents are not allowed: isopentylamino, isopentyl-methylamino, isobutyl-methylamino or amino.

29. Wu et al., U.S. Patent No. 6,191,166 does not anticipate the compounds and compositions of the present

invention because cannot represent $-\text{CH}(\text{CH}_3)-\text{CO}-\text{NH}-\text{CH}(\text{CO}_2\text{Me})$ as C_3-C_{12} -alkylene in the definition of D may not be substituted by methoxycarbonyl.

30. As outlined above, none of the cited prior art documents anticipate claim 55. Accordingly, the claim objection by the Examiner is obviated.

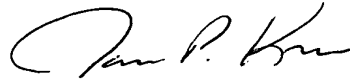
31. It is disagreed with the Examiner that U.S. Patent No. 6,313,153 discloses subject matter which is similar or identical to the claims of the present invention. In this connection, the Examiner's attention is drawn to the disclaimer in claim 1 of this document wherein it is explicitly stated that "AR¹ is not a 3-pyridyl group". Therefore, no overlapping subject matter between this U.S. patent and the pending claim exists.

The Commissioner is hereby authorized to charge any additional fees which may be required in this application to Deposit Account No. 06-1135.

Respectfully submitted,

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Date: DEC 10 2003

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